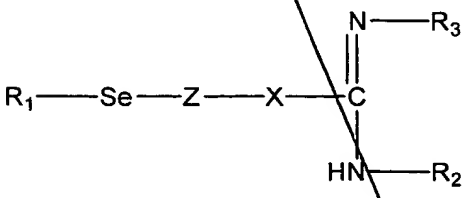
CLAIMS

1. Use of at least one molecule containing selenium, in a quantity corresponding to a daily dose of about 2 to 80 mg of atomic selenium equivalent, i.e about 0.025 to 1 mg/kg, for the production of a drug for treating severe systemic inflammatory response syndrome or any state corresponding to a severe acute attack of an inflammatory pathology causing an exacerbation of cytokine secretion, with the exception of a molecule of formula



in which :

R_1 is H, alkyl, alkenyl, phenyl, alkylene, alkenylene or phenylalkylene or a substituted derivative of these;

when R_1 is alkylene or alkenylene, R_1 may be bonded to the amidino group, to Z or to X to form a heterocyclic ring with 5, 6 or 7 members, provided that when R_1 is bonded to the Z group, Z is an alkylene or an alkenylene or a substituted derivative of these, and, when R_1 is bonded to the X group, the X group represents CR_5 or N;

R_2 and R_3 are independently H, lower alkyl, alkenyl, alkylene, alkenylene, amino, phenyl or phenylalkylene, or a substituted derivative of these;

when R_2 is alkylene or alkenylene, R_2 may optionally be bonded to the imino N group located adjacent to the carbon atom of the amidino group to form a heterocyclic ring with 5 or 6 members;

Z represents an alkylene, alkenylene, cycloalkylene or cycloalkenylene group or a substituted derivative of these;

when R_2 or R_3 represents an alkylene or alkenylene, R_2 or R_3 may optionally be bonded to the adjacent Z group to form a heterocyclic ring with 5 or 6 members containing nitrogen and carbon atoms and additionally not more than one oxygen or sulfur atom provided that this heterocyclic group is optionally substituted by a lower alkyl, alkoxy, halo, hydroxy or amino group;

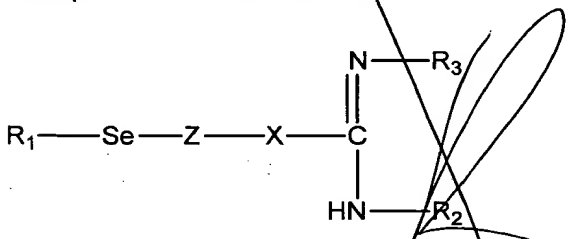
X represents N, NR_4, O, CR_5 or CR_4R_5;

R_4 represents H or an alkyl, thioalkylene or thioesteralkylene group;

R_5 represents H or an alkyl, alkylene, alkenylene, thioalkylene,

thioesteralkylene, amino or carboxyl group; and
when R_4 represents an alkylene, alkenylene, thioalkylene or thioesteralkylene group, R_4 may optionally be bonded to the R_2 or R_3 group to form a heterocyclic ring with 5 or 6 members containing nitrogen and carbon atoms and additionally not more than one oxygen or sulfur atom, on condition that R_2 and R_3 independently represent an alkylene, alkenylene, amino, phenyl, phenylalkylene or a substituted derivative of these in which the substituted derivative is a lower alkyl or halo group.

2. Use of at least one molecule containing selenium for the production of a drug for treating systemic inflammatory response syndrome, in a quantity corresponding to a daily dose of about 2 to 80 mg of atomic selenium equivalent, i.e. about 0.025 to 1 mg/kg, at the beginning of the treatment, then at a daily dose of about 0.5 to 2 mg of atomic selenium equivalent, with the exception of a molecule of formula



in which :

R_1 is H, alkyl, alkenyl, phenyl, alkylene, alkenylene or phenylalkylene or a substituted derivative of these;
when R_1 is alkylene or alkenylene, R_1 may be bonded to the amidino group, to Z or to X to form a heterocyclic ring with 5, 6 or 7 members, provided that when R_1 is bonded to the Z group, Z is an alkylene or an alkenylene or a substituted derivative of these, and, when R_1 is bonded to the X group, the X group represents CR_5 or N;

R_2 and R_3 are independently H, lower alkyl, alkenyl, alkylene, alkenylene, amino, phenyl or phenylalkylene, or a substituted derivative of these;
when R_2 is alkylene or alkenylene, R_2 may optionally be bonded to the imino N group located adjacent to the carbon atom of the amidino group to form a heterocyclic ring with 5 or 6 members;

Z represents an alkylene, alkenylene, cycloalkylene or cycloalkenylene group or a substituted derivative of these;
when R_2 or R_3 represents an alkylene or alkenylene, R_2 or R_3 may optionally be bonded to the adjacent Z group to form a heterocyclic ring with 5 or 6 members

containing nitrogen and carbon atoms and additionally not more than one oxygen or sulfur atom provided that this heterocyclic group is optionally substituted by a lower alkyl, alkoxy, halo, hydroxy or amino group;

X represents N, NR_4, O, CR_5 or CR_4R_5;

R_4 represents H or an alkyl, thioalkylene or thioesteralkylene group;

R_5 represents H or an alkyl, alkylene, alkenylene, thioalkylene, thioesteralkylene, amino or carboxyl group; and

when R_4 represents an alkylene, alkenylene, thioalkylene or thioesteralkylene group, R_4 may optionally be bonded to the R_2 or R_3 group to form a heterocyclic ring with 5 or 6 members containing nitrogen and carbon atoms and additionally not more than one oxygen or sulfur atom, provided that R_2 and R_3 independently represent an alkylene, alkenylene, amino, phenyl, phenylalkylene or a substituted derivative of these in which the substituted derivative is a lower alkyl or halo group in the subsequent treatment.

3. Use according to ~~one of claims 1 or 2~~ in which the drug is intended for treating severe acute infectious states, such as peritonitis, pneumopathies, meningitis or bacterial septicemias in a septic shock state.

4. Use according to ~~one of claims 1 or 2~~ for treating severe infectious states whether of bacterial, parasitic, fungal, or viral origin and, in general, any condition accompanied by a significant immuno-inflammatory reaction with in particular an increase in circulating cytokines, but also more localized conditions such as an attack of rheumatoid polyarthritis.

5. Use of the drug according to ~~any one of the preceding claims~~ for treatment in man or animals, the doses per kg being, in animals, modulated according to the 50% lethal dose (LD 50) of the species in comparison with that of the human species.

6. Use according to ~~any one of the preceding claims~~ in which the drug is produced so as to give a daily dose of about 2 to 80 mg of atomic selenium equivalent, i.e about 0.025 to 1 mg/kg, during the first day, and optionally the second, third and fourth days of treatment.

7. Use according to ~~any one of the preceding claims~~ in which the drug is produced so as to give a daily dose of about 0.5 to 2 mg of atomic selenium equivalent for 1 to 20 days during the subsequent treatment.

8. Use according to ~~any one of the preceding claims~~ according to which one of the molecules containing selenium is sodium selenite.

9. Use according to ~~any one of the preceding claims~~ in which several

molecules containing selenium are used simultaneously to modulate more precisely different compartments of the systemic inflammatory reaction.

10. Use according to claim 9 in which said molecules are one or more of the following molecules : a selenium salt, such as a selenite or selenate of inorganic selenium, or an organic selenium, for example selenocysteine, selenomethionine, selenodiglutathione, selenomethyl selenocysteine, dimethyl selenoxide, selenocystamine, selenated yeasts or synthetic chemicals containing one or more atoms of selenium, the preferred molecule being sodium selenite

11. Use according to ~~any one of the preceding claims~~ claim 1, characterized in that the drug is in a form which may be administered by the parenteral route, preferably by intravenous, and also by subcutaneous, intramuscular, and also by intraperitoneal, enteral or oral routes, and advantageously in an injectable or perfusable pharmaceutical form or for enteral administration.

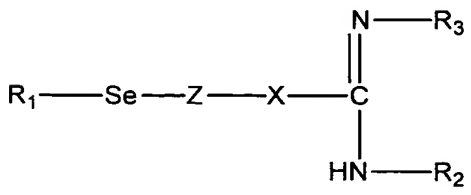
12. Use according to ~~any one of the preceding claims~~ claim 1, characterized in that the drug contains at least one associated non-selenium compound inhibiting, or reducing the consequences of, oxidative metabolism or inhibiting the inflammatory reaction.

13. Use according to claim 12, characterized in that the associated non-selenium compound which inhibits oxidative metabolism is selected from a glutathione precursor, an iron chelator, a copper chelator, copper, zinc, vitamin E and optionally vitamin C.

14. Use according to claim 12, characterized in that the compound inhibiting the inflammatory reaction is gold.

15. Use according to ~~any one of the preceding claims~~ claim 1, characterized in that the drug contains an essential oligo-element other than selenium or those cited above (Cu, Zn).

16. Pharmaceutical composition characterized in that it comprises a quantity of molecule or molecules containing selenium corresponding to a daily dose of about 2 to 80 mg of atomic selenium equivalent, i.e. about 0.025 to 1 mg/kg, and pharmaceutically acceptable excipients, with the exception of a molecule of formula



in which :

R_1 is H, alkyl, alkenyl, phenyl, alkylene, alkenylene or phenylalkylene or a substituted derivative of these;

when R_1 is alkylene or alkenylene, R_1 may be bonded to the amidino group, to Z or to X to form a heterocyclic ring with 5, 6 or 7 members, provided that when R_1 is bonded to the Z group, Z is an alkylene or an alkenylene or a substituted derivative of these, and, when R_1 is bonded to the X group, the X group represents CR_5 or N;

R_2 and R_3 are independently H, lower alkyl, alkenyl, alkylene, alkenylene, amino, phenyl or phenylalkylene, or a substituted derivative of these;

when R_2 is alkylene or alkenylene, R_2 may optionally be bonded to the imino N group located adjacent to the carbon atom of the amidino group to form a heterocyclic ring with 5 or 6 members;

Z represents an alkylene, alkenylene, cycloalkylene or cycloalkenylene group or a substituted derivative of these; when R_2 or R_3 represents an alkylene or alkenylene, R_2 or R_3 may optionally be bonded to the adjacent Z group to form a heterocyclic ring with 5 or 6 members containing nitrogen and carbon atoms and additionally not more than one oxygen or sulfur atom provided that this heterocyclic group is optionally substituted by a lower alkyl, alkoxy, halo, hydroxy or amino group;

X represents N, NR_4, O, CR_5 or CR_4R_5;

R_4 represents H or an alkyl, thioalkylene or thioesteralkylene group;

R_5 represents H or an alkyl, alkylene, alkenylene, thioalkylene, thioesteralkylene, amino or carboxyl group; and

when R_4 represents an alkylene, alkenylene, thioalkylene or thioesteralkylene group, R_4 may optionally be bonded to the R_2 or R_3 group to form a heterocyclic ring with 5 or 6 members containing nitrogen and carbon atoms and additionally not more than one oxygen or sulfur atom' provided that R_2 and R_3 independently represent an alkylene, alkenylene, amino, phenyl, phenylalkylene or a substituted derivative of these in which the substituted derivative is a lower alkyl or halo group..

17. Pharmaceutical composition according to claim 16, characterized in that it contains at least one associated non-selenium compound inhibiting or reducing the consequences of oxidative metabolism or inhibiting the inflammatory reaction.

18. Pharmaceutical composition according to claim 17, characterized in

that the associated non-selenium compound is selected from vitamin E and optionally vitamin C, a glutathione precursor, an iron chelator, a copper chelator, copper, or zinc.

19. Pharmaceutical composition according to claim 17, characterized in that the compound inhibiting the inflammatory reaction is gold.

20. Composition according to ~~any one of claims 16 to 19,~~ characterized in that it contains an essential oligo-element other than selenium or those cited above (Cu, Zn).

21. Composition according to ~~any one of claims 16 to 20,~~ characterized in that it is in an injectable or perfusable form or for parenteral administration, preferably intravenous (also subcutaneous or intramuscular), but also intraperitoneal, enteral or oral.

22. Composition according to ~~any one of claims 16 to 21,~~ characterized in that it is in the form of a perfusion containing between about 1.3 and 800 mg of atomic selenium equivalent per litre.

amendment by substitution of the pages, only claims 1-22 remain pending in this application.

Respectfully submitted,

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By _____

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